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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,799	08/29/2003	Patricia B. Hoyer	241331US20	7462

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/650,799	HOYER ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *3,7,14-19,26,27,31-36,39,44 and 48-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,9-13,20-25,28-30,37,38,41-43 and 45-47* is/are rejected.

7)☒ Claim(s) *8 and 40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/04,04/05,06/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I in the reply filed on 04/17/2006 is acknowledged. Applicant has elected the species 4-vinylcyclohexene diepoxide (VCD) and thus, as set forth in the paragraph bridging pages 2-3 of the restriction requirement dated 03/15/2006, claims that fail to read on the species VCD will not be considered at this time, including claims 3,7,26,27,39,44,48,58 and 59.

Claims 3,7,14-19,26,27,31-36,39,44 and 48-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 03/15/2006.

Claims 1-60 are pending and claims 1,2,4-6,8-13,20-25,28-30,37,38,40-43 and 45-47 are under consideration in the instant office action.

Information Disclosure Statement

The information disclosure statement filed 06/07/2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The poster listed as reference AAJ at page 4 on the IDS submitted 06/07/2004 is not legible and has not been considered in the instant office action.

Claim Objections

Claims 8,22 and 40 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Double Patenting

Applicant is advised that should claim 37 be found allowable, claim 45 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37,38,40,45,46 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37 and 45 are unclear because the method steps of claims 37 and 45 fail to relate back to the preamble in a positive process. The claim does not recite what is indicative of the desired outcome or what assay should be performed to complete the method. As such, the claims are unclear as to the metes and bounds of the phrase "an effective amount" because claims 37

and 45 fail to recite in the body of the claim what the compound must be effective in doing. Claims 38 and 40 depend from claim 37. Claims 46 and 47 depend from claim 45.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

1) Claims 1,2,4-6,9-10,13,23,24 and 28-30 are rejected under 35 U.S.C. 102(a) as being anticipated by Mayer et al. (Abstract of Poster Presentation presented at the Mountain West Society for Toxicology Meeting, Taos New Mexico, September 2001, IDS).

Mayer *et al.* taught administering 4-vinylcyclohexene diepoxide (VCD) to female mice at a dosage of 160 mg/kg daily for 15 days, resulting in follicle depletion. The mice are models of peri-menopause as evidenced by the absence of small pre-antral follicle pools and reduction of antral follicles (see specification at page 12, lines 16) and menopause.

Therefore, Mayer taught the limitations of claims 1,2,4-6,9-10,13,23,24 and 28-30.

2) Claims 1,2,4-6,9-13,23-25 and 28-30 are rejected under 35 U.S.C. 102(a) as being anticipated by Mayer et al. (Abstract of Poster Presentation presented at the Endocrinology Annual Meeting, San Francisco, CA, June 2002, IDS).

Mayer *et al.* taught administering 4-vinylcyclohexene diepoxide (VCD) to female mice at a dosage of 160 mg/kg daily, i.p., for 15 days, resulting in follicle depletion. The mice

exhibited of primary and primordial follicles and a reduction in secondary and antral follicles. VCD treatment resulted in loss of ovarian cyclicity and increased FSH levels, indicators of perimenopause and menopause.

Therefore, Mayer taught the limitations of claims 1,2,4-6,9-13,23-25 and 28-30.

3) Claims 41 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Acarturk (**Pharmaceutical Research**, 13:779-789, 1996).

Claims 41 and 43 require administering and effective amount of VCD to an animal population sufficient to cause ovarian failure in at least a portion of the population.

Kao et al. taught administering 80 mg/kg/day of VCD to cause menopause (ovarian failure, see page 3, line 12 of specification) in mice and rats. Kao et al. taught administering the VCD to multiple mice and rats, constituting a population as required by claim 41.

Therefore, Kao et al taught the limitations of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1) Claims 1 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kao et al. (1999, IDS) in view of Mayer et al. (2001, IDS) or Mayer et al (2002, IDS).

Claim 1 is drawn to a mammalian non-human female having at least partial depletion of the ovarian primordial follicles and at least one characteristic of menopause or perimenopause induced by administration of VCD at a dosage of 100mg/kg/day. Claim 20 limits the animal to a rat.

Kao et al. taught administering 80 mg/kg/day of VCD to cause characteristics of ovarian failure in mice and rats. Kao taught that mice appear to be more susceptible than rats to the ovotoxic effects of VCD. Kao et al. did not teach use of a dosage of at least 100mg/kg/day.

However, Mayer *et al.* (2002) taught administering 4-vinylcyclohexene diepoxide (VCD) to female mice at a dosage of 160 mg/kg daily for 15 days, resulting in follicle depletion. The mice exhibited of primary and primordial follicles and a reduction in secondary and antral follicles. VCD treatment resulted in loss of ovarian cyclicity and increased FSH levels, indicators of perimenopause and menopause. Similarly, Mayer *et al.* (2001) taught administering 4-vinylcyclohexene diepoxide (VCD) to female mice at a dosage of 160 mg/kg daily for 15 days, resulting in follicle depletion. The mice are models of peri-menopause as evidenced by the absence of small pre-antral follicle pools and reduction of antral follicles (see specification at page 12, lines 16) and menopause.

Therefore, it would have been obvious to combine the teachings of Kao et al with those of either of Mayer (2001) and Mayer et al (2002) to make a rat model of menopause to study the effects of VCD on premature menopause and the physiological processes involved in mammalian menopause using a rat as taught by Kao et al, using the 100mg/kg/day dosage taught by Mayer et al (2001) and Mayer et al (2002). One of skill in the art would be motivated to

combine such teachings to increase the desired menopausal characteristics especially in light of the teachings of Kao et al that rats are not as susceptible as mice to the toxic effects of VCD.

One of skill in the art would have had a reasonable expectation of success in applying the method of Mayer et al. (2001) or Mayer et al (2002) to rats because the anatomical and physiological processes that occur before and after the onset of menopause are similar in mice and rats, because Kao had demonstrated similar effects with 80mg/kg/day of VCD and because Mayer et al. (2001) and Mayer et al (2002) demonstrated no additional side effects of the higher dosage in mice.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

2) Claims 1 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abel *et al.* (**Jour Clin Endocrin Metab,** 84:2111-2118, 1999) in view of Mayer et al. (2001, IDS) or Mayer et al (2002, IDS) and further in view of Judd (1976, IDS).

Claim 1 is drawn to a mammalian non-human female having at least partial depletion of the ovarian primordial follicles and at least one characteristic of menopause or perimenopause induced by administration of VCD at a dosage of 100mg/kg/day. Claim 21 limits the animal to a primate.

Abel taught use of primates in generating animal models of menopause by ovarectomy for use in testing hormone replacement therapy. Abel did not teach administering VCD at a dosage of 100mg/kg/day to induce menopause.

However, Mayer *et al.* (2002) taught administering 4-vinylcyclohexene diepoxide (VCD) to female mice at a dosage of 160 mg/kg daily for 15 days, resulting in follicle depletion. The mice exhibited of primary and primordial follicles and a reduction in secondary and antral follicles. VCD treatment resulted in loss of ovarian cyclicity and increased FSH levels, indicators of perimenopause and menopause. Similarly, Mayer *et al.* (2001) taught administering 4-vinylcyclohexene diepoxide (VCD) to female mice at a dosage of 160 mg/kg daily for 15 days, resulting in follicle depletion. The mice are models of peri-menopause as evidenced by the absence of small pre-antral follicle pools and reduction of antral follicles (see specification at page 12, lines 16) and menopause. Mayer et al (2001) and Mayer et al (2002) each taught that VCD is an occupational chemical.

Furthermore, Judd (1976) taught that ovarectomy is not the best model of menopause as it lacks the hormonal regulation of the postmenopausal ovary as evidence by differences in hormone levels of normal postmenopausal women and women who have undergone ovarectomy.

Therefore, it would have been obvious to combine the teachings of Abel with those of either of Mayer (2001) and Mayer et al (2002) to make a primate model of menopause to study human post-menopausal hormone replacement therapies as taught by Abel by substituting ovarectomy with VCD treatment as taught by Mayer et al (2001) and Mayer et al (2002). One of skill in the art would be motivated to induce menopause in primates using VCD rather than ovarectomy because Judd taught that ovarectomy was not an exact model of menopause as it remove the active influences and functions of the post-menopausal ovary.

One of skill in the art would have had a reasonable expectation of success in applying the method of Mayer et al (2001) and Mayer et al (2002) to primates because primates are similar to

mice in the anatomical and physiological processes that occur before and after the onset of menopause.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

3) Claims 37,38,41-43 and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Acarturk (Pharmaceutical Research, 13:779-789, 1996) in view of Kao et al. (1999, IDS) and further in view of Judd (1976, IDS).

Claims 37 and 38 are drawn to a method of inducing ovarian failure comprising administering an effective amount of VCD to a mammal other than mouse or rat. The claims do not recite what the administration of VCD must be effective in causing. Claims 41-43 require administering and effective amount of VCD to an animal population sufficient to cause ovarian failure in at least a portion of the population. Claim 42 limits the animal species to a list of species that does not include mouse or rat. Claims 45-47 are drawn to a method of inducing sterilizing a mammal other than a mouse or rat comprising administering an effective amount of VCD to a mammal other than mouse or rat. The claims do not recite what the administration of VCD must be effective in causing.

Acarturk taught use of a rabbits in generating animal models of menopause by ovarectomy. Acarturk did not teach use of VCD in causing menopause or menopausal characteristics in rabbits.

However, Kao et al. taught administering 80 mg/kg/day of VCD to cause characteristics of ovarian failure in mice and rats. Kao et al. taught administering theVCD to multiple mice and

rats, constituting a population as required by claim 41. Ovarian failure inherently causes sterility as recited in the preamble of claim 45. Kao et al did not teach use of such a method in any other animal as required by the claims.

Furthermore, Judd (1976) taught that ovarectomy is not the best model of menopause as it lacks the hormonal regulation pf the postmenopausal ovary as evidence by differences in hormone levels of normal postmenopausal women and women who have undergone ovarectomy.

Therefore, it would have been obvious to combine the teachings of Acarturk et al with those of Kao et al. to make a rabbit model of menopause to study the effects of menopause on the mammal as taught by Acarturk by substituting ovarectomy with VCD treatment as taught by Kao. One of skill in the art would be motivated to induce menopause in the rabbit using VCD rather than ovarectomy because Judd taught that ovarectomy was not an exact model of menopause as it remove the active influences and functions of the post-menopausal ovary.

One of skill in the art would have had a reasonable expectation of success in applying the method of Kao to rabbits because Kao demonstrated that the method works on two rodent models and rabbits are rodents similar to rats and mice in the anatomical and physiological processes that occur before and after the onset of menopause.

Thus, the claimed invention is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Valarie Bertoglio
Examiner
Art Unit 1632